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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,308	01/10/2001	Howard A. Fields	14114.0349U2	9952

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EXAMINER	
LI, BAO Q	
ART UNIT	**PAPER NUMBER**
1648	11

DATE MAILED: 09/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,308	FIELDS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 14-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13 and 26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 7-31 are pending.

Response to Amendment

This is a response to the amendment, paper No. 9, filed 07/18/02. Claims 7 and 13 are amended. New claims 26-31 are added. Claims 7-13 and 26-31 are considered .

This application contains claims 1-6 and 14-25 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims 1-6 and 14-25 or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

New Matter

1. The amended claim 7 filed with amendment B, paper No. 9 on July 18, 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure is as follows: wherein at least two antigenic epitopes are from the same region of variants of the same protein."

Claim Rejections - 35 USC § 112

2. Claims 7 and 26 are still rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention on the same ground as stated in the previous office action.

For the rejection of claims 7-13 and 26-31 on the issue of the undefined metes and bonds of " one or more antigen epitopes", Applicants explained that the claims are not vague nor indefinite because the citation of one or more antigenic epitopes of each of the HCV antigens should be given their broadest possible meaning, namely, that the polypeptide of the invention includes at least one antigenic epitope from each of the protein listed. The metes and bonds of the invention are clear, precise and defined, particularly in light of the content of the application, the teaching of the prior art.

Applicants' argument has been fully considered; however, it is not found persuasive because HCV is a big family of virus, the virus sequences can be divided into major types (identified by numbers, such as 1, 2 or 3) with nucleotide identities of <70% over complete genome sequences. Each type can be subdivided into subtypes (identified by letters, i.e. a, b, or c) with identities of between 70 and 80%. It is also well known that being an RNA virus, HCV can mutate rapidly and automatically in adapting to the environments, thus contributing to the high genome divergence and quasispecies for multiple isolated viral strains in the world. A single isolated HCV strains even can generate more than a hundred clones in the most genetically heterogeneous region and each clone exhibits different immunogenecities. Furthermore, in light of the art, each genome of HCV core, NS3-5 protein ranges couple hundreds to more than thousand of nucleotides long, there are many epitopes has been identified and constructed as an antigenic peptide or polypeptide. Therefore, the word "comprising" used in the claims fails to define how each of the HCV antigenic proteins are constructed and which precise amino acid sequence structure is intended. If Applicants wish to claim a unique antigenic peptide of polypeptide of a particular HCV, the claims should use more defined language to describe precisely sequence of each HIV antigenic peptide or polypeptide and/or the precise epitope sequence that are intended. Otherwise, the rejection is maintained.

Claim Rejections - 35 USC § 102

3. Claims 7 and 26 are still rejected under 35 U.S.C. 102(b) as being anticipated by Chien et al. (a) (P.N.A.S. USA. 1992, Vol. 89, pp. 10011-10015) on the same ground as stated in the previous office action.

Applicants submit that Chien et al. (a) does not anticipate the claims because claim 7 is amended as ".... Wherein at least two antigenic epitopes are from the same region of variants of the same protein." Whereas, the disclosure of Chien et al. do not have this limitation.

Applicants further explained that "the different antigenic epitopes contemplated include those wherein the epitopes are derived from the same region of the same protein from different species". Applicants indicated that the support for the amendment of claim 7 can be found on

page 2, lines 23-29 and the support for "variants of the same protein" are disclosed on page No. 26, lines 21-31.

Applicants' argument has been fully considered; however, it is not found persuasive because the specification of page 2, lines 23-29 and page 26, lines 21-31 have been carefully viewed, it is the examiner's opinion that specification does not provide the support for this amendment.

The disclosure of page 2, lines 21-29 teach " *the mosaic polypeptide of the present application are artificial composite proteins constructed from different HCV proteins. Preferably from the core protein, NS3, and NS4. The preferred mosaic polypeptides optionally contain an additional antigen epitope from either the NS4 protein or the NS5a protein or both. Most preferably, the antigenic epitope of the core protein contains amino acid residue 1-91 of the HCV polypeptide (SEQ ID NO: 1), the antigenic epitope of the NS3 protein contains the amino acid residues 1471-1573 of the HCV polypeptide (SEQ ID NO: 2); the antigenic epitope of the preferred NS4 protein contains amino acid residues 1789-1867 of the HCV polyprotein (SEQ ID NO: 3); the antigenic epitope of the optional NS4 protein contains amino acids residues 1916-1948 of the HCV polypeptide (SEQ ID NO: 4); and the antigenic epitope of the optional NS5a protein contains amino acid residues 2333-2423 of the HCV polypeptide (SEQ ID NO: 5). The antigenic epitopes can be places in any order within the mosaic polypeptide*".

It is clear from the above disclosure that specification only teaches that epitopes that constitute the claimed mosaic peptide are selected and reconstructed from the disclosed SEQ ID NO: 1-5. According to the specification, all 5 sequences are all from HCV genotype 1b. There is no indication that the epitopes of claimed mosaic peptide of HCV are selected and reconstructed from different species of the HCV family.

The disclosure of page 26, line 21-31 teach that " *Antibodies are raised to the antigenic epitopes and mosaic polypeptides, including individual, allelic, strain, or species variants, and fragments thereof, both in their naturally occurring (full-length) forms and in recombinant forms. Additionally, antibodies are raised to these peptides in either their native configurations or in non-native configurations. Anti-idiotypic antibodies can also be generated. Many methods of making antibodies are known to persons skilled in the art. The following discussion is presented as a general overview of the techniques available; however, one of the skill will*

recognized that many variations upon the following methods are known." Applicants further explain that " *A number of immunogens are used to produce antibodies specifically reactive with peptides. Recombinant or synthetic peptides of ten amino acids in length, or greater, selected from subs-sequences of the antigenic epitopes and mosaic polypeptides disclosed herein are the preferred peptide immunogens for the production of monoclonal or polyclonal antibodies. In one class of proffered embodiments, an immunogenic peptide conjugate is also included as an immunogen. Naturally occurring peptides are also used whether in pure or impure form. Recombinant peptides are expressed in eukaryotic or prokaryotic cells and purified using standard techniques. The peptide, or a synthetic version thereof, is then injected into an animal capable of producing antibodies.*"

It is clear that the disclosure above only teach the specificity of an HIC antibody against an epitope antigen of HCV can be varied from strain to strain, the allelic to allelic and species to species. There is no teaching that the claimed mosaic polypeptide are made by a combination of at least two antigenic epitopes that are isolated from the same region of the same protein of different species.

According to the specification, the disclosed sequences of SEQ ID NO: 1-5 are all derived from one single strain of the HCV genotype 1b. The variation as taught by specification may be a combination that is derived from the sub-sequence of the combination of SEQ ID NO: 1-5 because Applicants teach that "*Recombinant or synthetic peptides of ten amino acids in length, or greater, selected from subs-sequences of the antigenic epitopes and mosaic polypeptides disclosed herein are the preferred peptide immunogens for the production of monoclonal or polyclonal antibodies.*" Applicants also emphasized that " *Most preferably, the antigenic epitope of the core protein contains amino acid residue 1-91 of the HCV polypeptide (SEQ ID NO: 1), the antigenic epitope of the NS3 protein contains the amino acid residues 1471-1573 of the HCV polypeptide (SEQ ID NO: 2); the antigenic epitope of the preferred NS4 protein contains amino acid residues 1789-1867 of the HCV polyprotein (SEQ ID NO: 3); the antigenic epitope of the optional NS4 protein contains amino acids residues 1916-1948 of the HCV polypeptide (SEQ ID NO: 4); and the antigenic epitope of the optional NS5a protein contains amino acid residues 2333-2423 of the HCV polypeptide (SEQ ID NO: 5).*"

Because the specification does not teach the limitation that mosaic polypeptide contains at least two antigenic epitopes from different species, the newly submitted amendment is a new matter, and it is not entered. The rejection over Chien et al. (a) is therefore, maintained.

4. Claims 7, 8 and 26 are still rejected under 35 U.S.C. 102(b) as anticipated by Chien et al. (b) (J. Gastro. Hepto. 1993, Vol. 8, pp. S33-39) on the same ground as stated in the previous office action.

Applicants submit the same arguments based on the newly amended claim 7, which applicants argue that is able to establish the Patentable distinctive over Chien et al. (a) and is also applicable for rebottle over the reference of Chien et al. (b). In addition, Applicants asserted that the C25 fusion protein only contains HCV core, NS3 and NS4, but not NS5, therefore, it cannot anticipated claims 7 and 8.

Applicants' argument has been fully considered, however it is not found persuasive because applicants fails to provide the support of the amendment of the claim 7 as described supra.

Furthermore, the six proteins polypeptide disclosed by Chien et al. (b) comprises the structural regions of core (C22-3), the envelope (E1 and E2) and non-structural regions NS3 (C33C)and NS3-NS4 (C11-3) and NS5. Therefore, it anticipated the claims 7, 8 and 26. Whereas, the seventh protein only contains non-structural regions NS3 (C33C) and NS3-NS4 (C11-3), it anticipated the claim 7. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

5. Claims 7, 9-12 and 26-31 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (a) (P.N.A.S. USA. 1992, Vol. 89, pp. 10011-10015) and Kato et al. (P.N.A.S. USA. 1990, Vol. 87, 9524-9528).

On the one hand that Applicants argue that the sequences cited in the references have no disclosure to have 100% homology to the sequences as disclosed in the claims.

On the other hand, Applicants asserted that the characterization of the present invention as being a particular sequence is too narrow. The present invention is not limited to any specific

subset of the core, such as amino acid residues 1-91; the NS3 protein, such as amino acid residues 1417-1573,; or the NS4 protein, such as 1789-1867 and 1916-1948. The present invention as recited in the amended claim 7 can include any antigenic epitope from HCV core protein, NS3 protein or NS4 protein so long as at least one antigen epitope is included from each and wherein at least two antigenic epitopes are from corresponding regions of variants of the core protein, NS3 protein and NS4 protein.

In response to applicant's argument that the references fail to show certain features of applicant's invention, such as the sequences cited in reference of Chien et al. and Kato et al, it is noted that the features upon which applicant relies (i.e., the SEQ ID NO: NO: 1-5) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, because the scope of the claimed invention can be explained as an epitope derived from any HCV core protein of amino acid residues 1-91; the NS3 protein of amino acid residues 1417-1573; the NS4 protein of amino acid residues of 789-1867 and 1916-1948; and amino acid residues 2322-2423 of NS5, the reference of Chien et al. (a) does teach the limitation of the claimed invention because the C25 protein comprises the epitopes of a HCV core protein, NS3 and NS4 proteins due to they are all located in the same range of claimed HCV proteins of core and NS3-5.

Applicants are reminded that the arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In the instant case, it is well known in the art prior to the application was filed teaches that HCV genome comprising many immune epitopes in the regions of HCV core protein, E1, E2 envelope proteins and non-structural proteins NS3, NS4 and NS5, and different antigenic peptide or polypeptide induce different kinds of antibodies or different antibodies recognize different antigenic epitopes as indicated by Chien et al. because they teach that structural protein C and non-structural HCV NS3-5 were found to contain the most immunodominant epitopes (Abstract). They further teach that the C100-3 antigen (NS4) represents only about 20% of the coding capacity of HCV and the anti-C100-3 assay is not capable of detecting all infectious blood donors (lines 7-15 on col. 2 of page 10011). They also demonstrated that the use of C25 polypeptide comprising HCV C22 antigen, C33C NS3 and C1-3 NS4 is able to get more positive anti-HCV antibody result. They indicated " in light of growing evidence fro substantial heterologenicity of the HCV genome, it was of important to determine the degree of crossreactivity of the constituent epitopes I the C25 antigen." They further suggested that the screening and diagnosis of HCV infection will be substantially enhanced through the use of multiple epitopes encoded by the chimeric C25 capture antigen. The development of additional assay for viral RNA and antigen should also be great value as will the development of viral-specific assay in order to investigate the potential influence of viral genotype on pathogenicity."

Therefore, it is still concluded that in order to get better sensitivity for detecting the HCV infection or get better immunogenicity for inducing an immune response, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Chien et al (a). and in further view of sequences the disclosed by Kato et al to make a mosaic polypeptide comprising HCV core, NS3 and NS4 for detecting more possible prevalence of the anti-HCV antibodies circulated in the patients. As there is no unexpected result, the claimed invention as a whole is prima facie obvious absence unexpected results.

6. Claims 7-13 and 26-31 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Chien et al. (b) (J. Gastro. Hepto. 1993, Vol. 8, pp. S33-39) and Kato et al. (P.N.A.S. USA. 1990, Vol. 87, 9524-9528) on the same ground as stated in the previous office action.

Applicants argue that there is not teaching from either Chien et al. (b) or Kato r et al. that the assay of Chien et al. is deficient or requires further sequence. Applicants further argue that there is no motivation to combine the elements that provide the present invention with expected success and the combination of the teaching much teach or suggest all claim limitations.

Applicants' argument has been fully considered, however, it is not found persuasive. Because the reference of Chien et al. teach that the fact of the more antigenic epitopes are used in the assay, the more sensitivity and specificity of antibodies that you are able to get. They demonstrated that polypeptide C25 assay, which is a multiple antigenic peptide derived from C, NS3, NS4 and NS5 of HCV, is superior to the single peptide assay of NS4. This is the motivation that promote an ordinary skill person in the art to use mosaic polypeptide comprising multiple epitopes from multiple regions of HCV, rather than a single peptide from on region of HCV, to do the assay to get more sensitive and specific detection of HCV antibodies with highly successful expectation.

The reference of Chien et al. (b) disclose to use the six proteins polypeptide disclosed comprises the structural regions of core (C22-3), the envelope (E1 and E2) and non-structural regions NS3 (C33C)and NS3-NS4 (C11-3) and NS5. it comprises the epitopes of the HCV core protein, NS3-NS5 proteins and they are all located in the range of claimed HCV antigenic proteins core, and NS3-5. Kato disclose whole amino acid sequence of a HCV.

Therefore, in order to get better sensitivity for detecting the HCV infection or get better immunogenicity for inducing an immune response, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Chien et al (b) and further in view of sequences disclosed by Kato et al to make a mosaic polypeptide comprising HCV core, NS3, NS4 and NS5 for detecting the anti-HCV antibodies with an improved higher sensitivity without unexpected results.

Because the claimed invention does not teach that the use of the claimed mosaic polypeptide of HCV is an unexpected result, which render much more significant sensitive and specific result over the prior art as disclosed in Chien et al. (b), it is still concluded that the claimed invention as a whole is prima facie obvious absence unexpected results.

7. Claims 7-13 and 26-31 are still rejected under 35 U.S.C. 103(a) as being unpatentable over Valenzuela et al. (WO 97/44469 A2) and in further view of Chien et al. (b) (J. Gastro. Hepto. 1993, Vol. 8, pp. S33-39) and Kato et al. (P.N.A.S. USA. 1990, Vol. 87, 9524-9528).

Applicants submit that the reference of Valenzuela et al. cannot be used for the basis of the rejection because the evidenced of the attached declaration of Harward and Yuri filed on paper No. under 37 C.F.R 1.131 on 8, July 18, 2002.

The Declaration filed on July 18, 2002 under 37 CFR 1.131 has been considered but is ineffective to overcome the Valenzuela et al.'s reference because the evidence submitted is insufficient to establish a reduction to practice of the invention in this country or a NAFTA or WTO member country prior to the effective date of the Valenzuela et al's reference filed on Nov. 27, 1999. Furthermore, the evidence submitted is insufficient to establish a conception of the invention prior to the effective date of the Valenzuela et al's reference filed on Nov. 27, 1999. While conception is the mental part of the inventive act, it must be capable of proof, such as by demonstrative evidence or by a complete disclosure to another. Conception is more than a vague idea of how to solve a problem. The requisite means themselves and their interaction must also be comprehended. See *Mergenthaler v. Scudder*, 1897 C.D. 724, 81 O.G. 1417 (D.C. Cir. 1897).

In the instant case, the claimed invention is drawn to a mosaic polypeptide comprising one or more antigenic epitopes of each of the hepatitis C virus (HCV), core protein, nonstructural protein 3 (NS3 protein) and nonstructural protein 4 (NS4 protein), optionally the epitope of polypeptide HCV NS5a protein. However, the document of COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT BETWEEN THE CNETERS FOR DISEASE CONTROL AND PREVENTION (CDA) AND BEOHRINGER MANNHEIN GmbH (BMG) Appendix B prepared prior to November 27, 1999, only discloses that the cooperation will involve the development of various artificial recombinant protein composed of broadly immunoreactive epitope. The protein is called "mosaic" protein because it is composed of a mosaic of antigenic epitopes. Furthermore, the Declaration teaches that " Recently, using 150 synthetic peptides spanning the entire HCV NS3-NS4, NS5 proteins, we have identified a large number of linear B-cell epitopes.

Therefore, it is clear that the achievement disclosed in the Declaration is different from the claimed invention. The reference of Valenzuela et al. is still eligible as a basis for the obviousness type rejection.

Valenzuela et al. teach a multiple copy epitope sequence having the general structural formular (I): (A)x-(B)y-(C)z, wherein the (I) is a linear amino acid sequence and the A. B. and C, are epitopes from the regions of the HCV polyprotein. The said regions are selected fro the group consisting of NS3, NS4, NS5, c100, C25, core, E1, E2, c33c, c100-3 and c22. Velenzuela et al. also disclose that the multiple epitope polypeptide are used as a composition for detecting the HCV infection (see claims 1, 5 and 12).

The reference of Chien et al. (b) disclose to use the six proteins polypeptide comprises the structural regions of core (C22-3), the envelope (E1 and E2) and non-structural regions NS3 (C33C)and NS3-NS4 (C11-3) and NS5. it comprises the epitopes of the HCV core protein, NS3 and NS4 proteins due to they are all located in the range of amino acid residues 1-91 of core, amino acid residues 1471-1573 of NS3 and amino acid residues 1789-1948 of NS4. Kato disclose the sequence including the all epitope of amino acid residues 2322-2423 of NS5. Chien et al. also demonstrate that the use of multiple antigenic peptides of C, NS3, NS4 and NS5 for detecting the antibodies is superior to use of the single peptide NS4 along. Therefore, it would have been motivated for an ordinary skill person in the art to use mosaic polypeptide comprising multiple epitopes from multiple regions of HCV, rather than single peptide from on region of HCV, to do the assay to get more sensitive and specific results with highly successful expectation.

Therefore, in order to get better sensitivity for detecting the HCV infection or get better immunogenicity for inducing an immune response, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited reference of Valezuela et al. and in further view of the teaching of Chien et al. (b) and Kato et al to make a mosaic polypeptide comprising multiple epitope from each of the regions of HCV to detect the different antibodies with an improved higher sensitivity.

Because there is no unexpected result claimed, it is still concluded that the claimed invention as a whole is prima facie obvious absence unexpected results.

New Grounds of Rejections:

Claim Rejections - 35 USC § 112

8. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, Applicants amended claim 7 as ".... Wherein at least two antigenic epitopes are from the same region of variants of the same protein." Applicants indicated that the support for the amendment of claim 7 can be found on page 2, lines 23-29 and the support for "variants of the same protein" are disclosed on page No. 26, lines 21-31.

The specification of page 2, lines 23-29 and page 26, lines 21-31 have been carefully viewed, the specification does not have the support that teaches the mosaic polypeptide contains at least two antigenic epitopes are from the same region of the same protein of different species. Applicants' argument has been fully considered; however, it is not found persuasive because the specification of page 2, lines 23-29 and page 26, lines 21-31 have been carefully viewed, it is the examiner's opinion that specification does not provide the support for this amendment.

The disclosure of page 2, lines 21-29 teach " *the mosaic polypeptide of the present application are artificial composite proteins constructed from different HCV proteins. Preferably from the core protein, NS3, and NS4. The preferred mosaic polypeptides optionally contain an additional antigen epitope from either the NS4 protein or the NS5a protein or both. Most preferably, the antigenic epitope of the core protein contains amino acid residue 1-91 of the HCV polypeptide (SEQ ID NO: 1), the antigenic epitope of the NS3 protein contains the amino acid residues 1471-1573 of the HCV polypeptide (SEQ ID NO: 2); the antigenic epitope of the preferred NS4 protein contains amino acid residues 1789-1867 of the HCV polyprotein (SEQ ID NO: 3); the antigenic epitope of the optional NS4 protein contains amino acids residues 1916-1948 of the HCV polypeptide (SEQ ID NO: 4); and the antigenic epitope of the optional NS5a protein contains amino acid residues 2333-2423 of the HCV polypeptide (SEQ ID NO: 5). The antigenic epitopes can be places in any order within the mosaic polypeptide*".

It is clear from the above disclosure that specification only teach that epitopes that constitute the claimed mosaic peptide are selected and reconstructed from the disclosed SEQ ID NO: 1-5. According to the specification, all 5 sequences are all from HCV genotype 1b. There is no indication that the epitopes of claimed mosaic peptide of HCV are selected and reconstructed from different species of the HCV family.

The disclosure of page 26, line 21-31 teach that " *Antibodies are raised to the antigenic epitopes and mosaic polypeptides, including individual, allelic, strain, or species variants, and fragments thereof, both in their naturally occurring (full-length) forms and in recombinant forms. Additionally, antibodies are raised to these peptides in either their native configurations or in non-native configurations. Anti-idiotypic antibodies can also be generated. Many methods of making antibodies are known to persons skilled in the art. The following discussion is presented as a general overview of the techniques available; however, one of the skill will recognized that many variations upon the following methods are known.*" Applicants further explain that " *A number of immunogens are used to produce antibodies specifically reactive with peptides. Recombinant or synthetic peptides of ten amino acids in length, or greater, selected from subs-sequences of the antigenic epitopes and mosaic polypeptides disclosed herein are the preferred peptide immunogens for the production of monoclonal or polyclonal antibodies. In one class of proffered embodiments, an immunogenic peptide conjugate is also included as an immunogen. Naturally occurring peptides are also used whether in pure or impure form. Recombinant peptides are expressed in eukaryotic or prokaryotic cells and purified using standard techniques. The peptide, or a synthetic version thereof, is then injected into an animal capable of producing antibodies.*"

It is clear that the disclosure above only teach the specificity of an HIC antibody against an epitope antigen of HCV can be varied from strain to strain, the allelic to allelic and species to species. There is no teaching that the claimed mosaic polypeptide are made by a combination of at least two antigenic epitopes that are isolated from the same region of the same protein of different species.

According to the specification, the disclosed sequences SEQ ID NO: 1-5 are all derived from one single strain of the HCV genotype 1b. The variation as taught by specification may be a combination that is derived from the sub-sequence of the combination of SEQ ID NO: 1-5

because Applicants teach that "*Recombinant or synthetic peptides of ten amino acids in length, or greater, selected from subs-sequences of the antigenic epitopes and mosaic polypeptides disclosed herein are the preferred peptide immunogens for the production of monoclonal or polyclonal antibodies.*" Applicants also emphasized that " *Most preferably, the antigenic epitope of the core protein contains amino acid residue 1-91 of the HCV polypeptide (SEQ ID NO: 1), the antigenic epitope of the NS3 protein contains the amino acid residues 1471-1573 of the HCV polypeptide (SEQ ID NO: 2); the antigenic epitope of the preferred NS4 protein contains amino acid residues 1789-1867 of the HCV polyprotein (SEQ ID NO: 3); the antigenic epitope of the optional NS4 protein contains amino acids residues 1916-1948 of the HCV polypeptide (SEQ ID NO: 4); and the antigenic epitope of the optional NS5a protein contains amino acid residues 2333-2423 of the HCV polypeptide (SEQ ID NO: 5).*"

Since the specification does not teach that the mosaic polypeptide contains at least two antigenic epitopes are from the same region of variants of the same protein, the newly submitted amendment is a new matter, and is rejected.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 8:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li
September 19, 2002